REMARKS

Claims 21-42 are currently pending in this application. Claims 21-26, 31-37, and 39-40 have been withdrawn. Claims 27-30, 38, 41, and 42 are presented for examination.

New claim 41 is supported on page 10, lines 35-36 of the specification. New claim 42 is supported on page 10, line 38 through page 11, line 3, of the specification. These new claims do not add new matter.

The Office rejected claims 27-30 and 38 under 35 U.S.C. § 112, second paragraph, because it asserted that the claims are indefinite. Specifically, the Office asserted that in claims 27-30 it is not clear what distinguishes the capture antibody from the revelation antibody. As indicated in the specification, there is no inherent characteristic that distinguishes the capture antibody from the revelation antibody, and in fact, they may be the same antibody. *See* specification at 8, lines 5-6.

The specification does describe ways in which the revelation antibody can be practically distinguished from the capture antibody, such as with a conjugated label either attached to the revelation antibody or attached to a third antibody that recognizes the revelation antibody. *See* on page 10, line 33 through page 11, line 32. Accordingly, claim 27 has been amended to indicate that the revelation antibody is "identifiable with a conjugated label." Embodiments of this label, either conjugated directly to the revelation antibody or to a third antibody that binds to the revelation antibody, are claimed in new claims 41 and 42. Applicants assert that amended claim 27, and claims 28-30 that depend from it, are definite under 35 U.S.C. § 112, second paragraph, and that the rejection should be withdrawn.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

The Office also rejected claim 38 under 35 U.S.C. § 112, second paragraph, asserting that it is incomplete without a step of selecting the antibodies. Applicants have amended claim 38 to include this step, and respectfully ask that the rejection be withdrawn.

The Office rejected claims 27-30 as being obvious in view of Zuk et al. and Crooks, et al. under 35 U.S.C. § 103. The Office asserted that Zuk et al. teaches kits with reagents for immunoassays, and that Crooks et al. teaches that antibodies to the NS1 protein bind to the hexameric form. Furthermore, the Office asserted that the specification teaches an immunoassay with antibodies for the detection of NS1 protein in its discussion of Falconar. The Office found that the combination of these disclosures renders the claims obvious.

Applicants traverse this rejection on the grounds that not all of the claim elements, specifically the elements of antibodies preselected as binding to or directed against the hexameric form of NS1, are recited in any of the disclosures cited. *See In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970) ("All words in a claim must be considered in judging the patentability of that claim against the prior art."). Claim 27 recites that the first, capture antibody is an antibody that is "preselected by immunocapture on the NS1 protein of the flavivirus, wherein the NS1 protein is in hexameric form" and the second, revelation antibody is an antibody "directed against a NS1 protein in hexameric form". These antibodies are not disclosed in Crooks et al. or in Falconar as discussed in the specification. While Crooks et al. identifies the hexameric form of NS1, and the Office noted that antibodies raised to NS1 protein would bind to the hexameric form, there is no disclosure of antibodies *preselected* to

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

bind this form or *directed against* this form in the references cited. Similarly, while the specification discusses previous studies of Falconar in which antibodies that bind NS1 are used, these antibodies are not *preselected* for or *directed against* the hexameric form of NS1. Finally, Zuk et al. does not discuss NS1 or antibodies directed to it in any form.

Furthermore, in the discussion of a report by Falconar, the specification notes that Falconar used a double-sandwich ELISA with antibodies directed against NS1 protein and that this assay "does not make it possible to detect the NS1 protein either in the case of primary infections in the acute or convalescent phase, or in secondary infections in the convalescent phase is which there is a high-titer of anti-NS1 antibodies . . . ." Specification at 6, lines 26 through 7, line 6. In contrast, the assay of the claimed invention, using antibodies selected with the hexameric form of the NS1 protein, can detect the virus in the early phases of infection, before a specific antibody response is detectable. *See* specification at 7, lines 18-28; *see also* Specification at Example 4, pgs. 25-26. Because the assay attributed in the specification to Falconar differs from that of the claimed invention and does not provide comparable results as the claimed invention, Falconar does not contribute to the obviousness of the invention.

Without disclosure of antibodies preselected or directed against the hexameric form of NS1, the claimed invention is not obvious. The specification describes the unexpected results and advantages of including antibodies selected for the hexameric form of the NS1 protein in boxed sets on pages 9 through 10. Briefly, the specification teaches that it was surprising to learn that an antibody raised to the hexameric form "makes it possible to significantly improve the sensitivity of the method and to detect the

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

NS1 protein circulating in the blood of patients." Specification at 9, line 32 through 10, line 3. The specification also indicates some of the advantages of using these antibodies, including the assay "may be carried out early, . . . is sensitive, . . . is rapid, . . . is relatively inexpensive, . . .[and] makes it possible to distinguish vaccinated individuals from individuals recently infected with a flavivirus." Specification at 10, lines 8-27. Because all of the elements of the assay in the boxed set claimed in claim 27, and therefore claims 28-20, which depend from claim 27, are not disclosed in the references provided by the Office, and the claimed invention would produce results that the disclosed elements would not, Applicants respectfully request that the rejection under 35 U.S. C. § 103 be withdrawn.

The Office also rejected claim 38 as being obvious in view of Zuk et al., Crooks et al., and Harlow et al., under 35 U.S.C. § 103. Applicants traverse this rejection because none of these references disclose how antibodies are selected that are "able to diagnose an infection with a flavivirus, at an early stage". As explained above, selection of antibodies against the hexameric form of NS1 allows the antibodies to detect infection at an earlier stage than can be detected with non-selected antibodies, as demonstrated by the comparison of the results reported in Falconar with those of the invention. *See* Specification at 6, lines 26 through 7, line 6; at 7, lines 18-28; and at Example 4, pgs. 25-26. Because none of the cited references disclose selection with the hexameric form of NS1, the references do not disclose all of the limitations of the claim. Applicants respectfully request that this rejection be withdrawn.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: September 26, 2003

By: _____

Deborah Katz
Reg. No. 51,863
Phone: (202) 408-4382
Fax: (202) 408-4400
E-mail: deborah.katz@finnegan.com

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com